

Application No. 10/530,552

Reply to Office Action

*AMENDMENTS TO THE SPECIFICATION*RECEIVED  
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Replace paragraph [0018] with:

[0018] Specific examples of such compounds are (2R,3R,4S,5R)-2-[2-chloro-6-(3-iodobenzylamino)purin-9-yl]-5-hydroxymethyltetrahydrothiophene-3,4-diol, (2R,3R,4S,5R)-2-(2-chloro-6-methylaminopurin-9-yl)-5-hydroxymethyl-tetrahydrothiophene-3,4-diol, ~~(2R,3R,4S,5R)-2-(2-chloro-6-methylaminopurin-9-yl)-5-hydroxymethyltetrahydrothiophene-3,4-diol~~ (2R,3R,4S,5R)-2-(2-chloro-6-aminopurin-9-yl)-5-hydroxymethyltetrahydrothiophene-3,4-diol, (2S,3S,4R,5R)-5-(6-amino-2-chloro-purin-9-yl)-3,4-dihydroxytetrahydrothiophene-2-carboxylic acid methyl amide, (2S,3S,4R,5R)-5-(2-chloro-6-methylaminopurin-9-yl)-3,4-dihydroxytetrahydrothiophene-2-carboxylic acid methyl amide, and (2S,3S,4R,5R)-5-[2-chloro-6-(3-iodobenzylamino)purin-9-yl]-3,4-dihydroxytetrahydrothiophene-2-carboxylic acid methyl amide.

Replace paragraph [00105] with:

[00105] ~~Experimental Example 25~~ *Experimental Example 25*. Synthesis of ~~(2R,3R,4S,5R)-2-(2-chloro-6-methylaminopurin-9-yl)-5-hydroxymethyltetrahydrothiophene-3,4-diol~~ (2R,3R,4S,5R)-2-(2-chloro-6-aminopurin-9-yl)-5-hydroxymethyltetrahydrothiophene-3,4-diol compound (25).

Replace paragraph [00106] with:

[00106] 5 mL of 80% aqueous acetic acid solution were added to 102 mg (0.22 mmol) of benzoic acid (3aS,4R,6R,6aR)-6-(6-amino-2-chloro-purin-9-yl)-2,2-dimethyltetrahydrothieno[3,4-d][1,3]dioxol-4-yl methyl ester, which was then stirred at 55°C for 12 h. The reaction mixture was distilled under reduced pressure, and then the pH of the concentrate was adjusted to neutral by adding saturated ammonia methanol solution. The concentrate was purified by silica gel column chromatography using the eluant (dichloromethane and methanol = 15:1) to obtain benzoic acid (2R,3S,4R,5R)-5-[6-amino-2-chloro-purin-9-yl]-3,4-dihydroxytetrahydrothiophen-4-yl methyl ester as white foam. The aforementioned benzoic acid (2R,3S,4R,5R)-5-[6-amino-2-chloro-purin-9-yl]-3,4-dihydroxytetrahydrothiophen-4-yl methyl ester was dissolved in 5 mL of methanol to which 15 mg (0.29 mmol) of sodium methoxide were added. The reaction mixture was stirred at

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ambient temperature for 4 h and the pH of the solution was adjusted to neutral with acetic acid, followed by distillation under reduced pressure. The concentrate was purified by silica gel column chromatography using the eluant (dichloromethane:methanol = 6:1) to obtain 37 mg (yield: 53%) of ~~(2R,3R,4S,5R)-2-(2-chloro-6-methylaminopurin-9-yl)-5-hydroxymethyltetrahydrothiophene-3,4-diol~~ (2R,3R,4S,5R)-2-(2-chloro-6-aminopurin-9-yl)-5-hydroxymethyltetrahydrothiophene-3,4-diol as white solids (see Table 3).

Melting point: 220-222°C

 $[\alpha]^{24}_D$ : -24.6 (c 0.7 methanol) $\nu_{\text{MAX}}$  (KBr)/cm<sup>-1</sup>: 1204, 1647, 3420<sup>1</sup>H-NMR(DMSO-d<sub>6</sub>)  $\delta$ : 3.30 (br s, 1H), 3.62 (m, 1H), 3.79 (m, 1H), 4.20 (dd, 1H), 4.61 (dd, 1H), 5.16 (t, 1H), 5.34 (d, 1H), 5.58 (d, 1H), 5.77 (d, 1H), 7.81 (br s, 2H), 8.48 (s, 1H)<sup>13</sup>C-NMR(DMSO-d<sub>6</sub>)  $\delta$ : 53.3, 61.2, 63.1, 73.1, 76.9, 118.0, 140.4, 150.7, 152.9, 156.7UV (methanol):  $\lambda_{\text{max}}$  264 nm (pH 7).